

Exhibit B:
Copy of Lab Notebook LB101
pages 125-135

Temperature Study (D067 v01)

Aim. To determine the budesonide content and related substances present in heat stressed samples of budesonide concentrations following D067 v01.

Patent. D067 v01

Methods. DTM003 v02.

Spec. N/A.

Analyt. PLAMR

Analyzed. [REDACTED]

Millenium Project. NPD2 - Budesonide.

Sample Set. 09-0018

Acquisition method. DTM003 Ver02

Process method. DTM003

Reporting method. DTM003 assay.

Sequence of Inj. Refer to raw data.

VOID

Temp Study.Concentrate Prep.

Concentrate A (37 mg/ml) - LB137 pg 7. Actual Conc 37.66 mg/ml.

Conc B (75 mg/ml) - LB137 pg 7. Actual Conc ^{Pl. [redacted]} 75.1422 mg/ml.

Conc C (75 mg/ml) - LB137 pg 7. Actual Conc 75.0982 mg/ml.

Conc D (150 mg/ml) - LB137 pg 7. Actual Conc 150.1612 mg/ml.
Note The above concentrates were separated and treated as below.

Treatment of concentrates.

A1 + A2 - Controls

A3 + A4 - Heated at 110°C for 120 mins

A5 + A6 - Heated at 121°C for 20 mins

A7 + A8 - Heated at 121°C for 30 mins.

B1 + B2 - Controls

B3 + B4 - Heated at 110°C for 120 mins

B5 + B6 - Heated at 121°C for 20 mins

B7 + B8 - Heated at 121°C for 30 mins

C1 + C2 - Controls

C3 + C4 - Heated at 121°C for 20 mins

D1 + D2 - Controls

D3 + D4 - Heated at 121°C for 20 mins.

Temp StudyStandard Preparation

Wk Std A. SS. [REDACTED].001.PL. SS042 pg 82.
10.01mg budesonide in stock std (99.8%)

Wk Std B. SS. [REDACTED].002.PL. SS042 pg 82
10.07mg budesonide in stock std (99.8%)

LoQ Solution. SS. [REDACTED].004.PL. SS042 pg 58
[REDACTED].007.PL. [REDACTED].

Sample Solutions

SS. [REDACTED].003-026.PL. SS.042 pg 85

Placebo. SS. [REDACTED].005.PL. SS042 pg 57

Band Sydes SS. [REDACTED].006.PL. SS042 pg 57.

HPLC Conditions

System. Waters system 9

Column. Waters symmetry C₁₈, 5μ, 150x3.9mm (SPOL 130)

Flow Rate. 1.5 ml/min

Inj Vol. 100μl.

Temp. 35°C

Detection. UV at 240 nm

Run Time. 35 min

Mobile Phase. RS0 [REDACTED].002.PL. RS026 pg 128

System suitabilityStandard A (vial 2) \bar{x} 12535253Standard B (vial 1)
(inj 2-c) \bar{x} 12594627 %RSD 0.2

$$\text{Std Recovery} = \frac{12535253 \times 10.07 \times 100}{12594627 \times 10.01} = 100.1\%$$

%RSD ($n=4$) \bar{x} (spec ≤ 0.2) 0.2%

Std Recovery (spec 98-102%) 100.1%

* USP Testing (r) (spec ≤ 2.0) Epimer A \bar{x} 1.15 Epimer B = 1.14* USP Resolution (R) (spec > 1.5) 1.82 \bar{x} 1.82Efficiency (plate number) \bar{x}

* Taken from standard b (vial 1) injection 2:

System suitability complies to requirements set
in DTM003 v2.

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Temp Study

Budesonide Content

Calculations:

Area Sam x Wstd x Vol Sam x P x Density

Area Std 100 W Sam 100

$$2506882.1 \times 10.01 \times 100 \times 99.8 \times 1.004 = 37.5775 \text{ mg/ml}$$

$$12572719 \quad 100 \quad 0.5322 \quad 100$$

$$\text{Std Recovery} = \frac{\text{Actual Conc} \times 100}{\text{Theor Conc}} = \frac{37.5775 \times 100}{37.667} = 99.8\%$$

Sample Run Sample ID	Total Budesonide	Peak Area Sample Wt	mg/ml	Actual Wt of Conc	% Concentrate
STD A	12516482		N/A		
STD A	12554024		N/A		
A1	25068821	0.5322	37.5775	37.687	99.8
A2	25055501	0.532	37.5717	37.687	99.7
A3	24907493	0.548	36.3920	37.687	96.8
A4	23999541	0.5209	36.7551	37.687	97.6
STD A	12609951		N/A		
STD A	12610419		N/A		
A5	24196025	0.5189	37.1835	37.687	98.7
A6	25078825	0.5373	37.2354	37.687	98.9
A7	25938036	0.5498	37.6358	37.687	99.8
A8	25062187	0.5384	37.2734	37.687	99.0
STD A	12606980		N/A		
STD A	12607422		N/A		
B1	26795641	0.2847	74.9571	75.1422	99.8
B2	26831103	0.287	74.4551	75.1422	99.1
B3	26676999	0.2781	74.9645	75.1422	99.6
B4	27290223	0.2931	74.1278	75.1422	98.6
STD A	12585416		N/A		
STD A	12576839		N/A		
B5	23714987	0.2641	74.4016	75.1422	99.0
B6	26389995	0.2741	73.8445	75.1422	98.3
B7	26916021	0.2859	75.0518	75.1422	99.9
B8	25422068	0.2704	74.9495	75.1422	99.7
STD A	12581243		N/A		
STD A	12583663		N/A		
C1	23813148	0.2519	75.2784	75.0982	100.2
C2	24662048	0.2619	74.9852	75.0982	99.8
C3	24129500	0.25	76.8582	75.0982	102.3
C4	26908820	0.3005	76.6068	75.0982	102.0
STD A	12607935		N/A		
STD A	12609307		N/A		
D1	23283410	0.2502	148.1188	150.1512	98.6
D2	22258643	0.2391	148.1733	150.1512	99.7
D3	23005685	0.2406	148.4884	150.1512	98.9
D4	23902695	0.2546	149.3132	150.1512	99.4
STD A	12594370		N/A		
STD A	12600801		N/A		

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P.L. N/A

Temp StudyRelated Subs

Calc.

Known Degr.

$$= \frac{A_{imp}}{A_{act}} \times RF \times 100.$$

A_{act}

$$RF - 16\% \text{ Hydro} - 0.89$$

$$- \text{Resonide} - 0.99$$

Example AI. - 16% Hydrox.

$$- 2,1\text{-Dehydro} - 1.56$$

$$= \frac{7741}{25068821} \times 0.89 \times 100 = 0.027\%$$

$$- 12\text{-Dihydro} - 0.96$$

25068821

$$- \text{Other knowns} - 1.00 *$$

* RF not calculated, taken to be 1.0.

Unknown Degr.

$$= \frac{A_{imp}}{A_{act}} \times 100$$

A_{act}

Example AI

Impurity at 34.0 mins (RRT = 2.13)

$$= \frac{415}{25068821} \times 100 = 0.016\%$$

25068821

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Temp Study

37 mg/ml Concentrate	Control		Heated at 110°C for 120Mins		Heated at 121°C for 20Mins		Heated at 121°C for 30Mins	
	A1	A2	A3	A4	A5	A6	A7	A8
16 α Hydropredisolone	0.027	0.030	0.024	0.021	0.048	0.043	0.031	0.035
Desonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
21-Dehydro-budesonide	0.054	0.046	0.119	0.083	0.065	0.074	0.077	0.072
Budesonide-12-dihydro	0.017	0.018	0.021	0.020	0.019	0.020	0.020	0.021
22-Methyl-Homologue of Budesonide	N.D.	N.D.	0.016	0.016	0.026	0.022	N.D.	N.D.
D-homobudesonide	0.022	0.022	0.020	0.019	0.021	0.020	0.021	0.021
14, 15-dehydrobudesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
S-11-keto budesonide	0.017	0.022	0.030	0.032	0.025	0.023	0.025	0.025
R-11-keto budesonide	0.022	0.023	0.032	0.036	0.031	0.030	0.030	0.031
S-21-acetate budesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
R-21-acetate budesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Total Known	0.054	0.00	0.119	0.083	0.065	0.074	0.077	0.072
Mean of Total Knowns	0.027		0.101		0.070		0.075	
Unknown 1 RRT 1.78	0.031	0.032	0.062	0.065	0.016	0.057	0.034	0.064
Unknown 2 RRT 2.13	0.016	N.D.	N.D.	0.013	N.D.	N.D.	N.D.	N.D.
Max Unknown	0.031 RRT 1.78	0.032 RRT 1.78	0.062 RRT 1.78	0.065 RRT 1.78	0.016 RRT 1.78	0.057 RRT 1.78	0.034 RRT 1.78	0.064 RRT 1.78
Total Unknown	0.00	0.00	0.062	0.065	0.00	0.057	0.00	0.064
Mean of Total Unknowns	0.00		0.064		0.029		0.032	
Total Impurities	0.054	0.00	0.181	0.148	0.065	0.131	0.077	0.136
Mean of Total Impurities	0.027		0.164		0.098		0.107	

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R.

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Project number

Temp Study

75 mg/ml Concentrate	Control		Heated at 110°C for 120Mins		Heated at 121°C for 20Mins		Heated at 121°C for 30Mins	
	B1	B2	B3	B4	B5	B6	B7	B8
16 α Hydroprednisolone	0.039	0.039	0.055	0.048	0.058	0.056	0.040	0.045
Desonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
21 - Dehydro - budesonide	0.026	0.026	0.042	0.060	0.025	0.029	0.070	0.065
Budesonide - 12 - dihydro	0.017	0.019	0.021	0.021	0.019	0.019	0.019	0.018
22 - Methyl - Homologue of Budesonide	0.023	0.024	0.042	0.034	0.043	0.037	0.019	0.026
D - homobudesonide	0.021	0.021	0.020	0.020	0.020	0.020	0.020	0.020
14, 15 - dehydrobudesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
S - 11 - keto budesonide	0.023	0.025	0.034	0.030	0.019	0.018	0.018	0.020
R - 11 - keto budesonide	0.029	0.029	0.033	0.035	0.043	0.024	0.024	0.024
S - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
R - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Total Known	0.00	0.00	0.055	0.060	0.058	0.056	0.070	0.065
Mean of Total Knowns	0.00		0.058		0.057		0.068	
Unknown 1 RRT 1.78	0.031	0.051	0.067	0.044	0.029	0.029	0.029	0.047
Unknown 2 RRT 2.13	0.016	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Max Unknown	0.031 RRT 1.78	0.051 RRT 1.78	0.067 RRT 1.78	0.044 RRT 1.78	0.029 RRT 1.78	0.029 RRT 1.78	0.029 RRT 1.78	0.047 RRT 1.78
Total Unknown	0.00	0.051	0.062	0.00	0.00	0.00	0.00	0.00
Mean of Total Unknowns	0.026		0.031		0.00		0.00	
Total Impurities	0.054	0.051	0.122	0.060	0.058	0.056	0.070	0.065
Mean of Total Impurities	0.053		0.091		0.057		0.068	

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Temp Study

75 mg/ml Concentrate	Control		Heated at 121°C for 20Mins	
	C1	C2	C3	C4
16 α . Hydropredisolone	0.044	0.053	0.054	0.046
Desonide	N.D.	N.D.	N.D.	N.D.
21 - Dehydro - budesonide	0.025	0.022	0.027	0.051
Budesonide - 12 - dihydro	0.020	0.020	0.022	0.023
22 - Methyl - Homologue of Budesonide	0.027	0.039	0.040	0.035
D - homobudesonide	0.021	0.021	0.020	0.020
14, 15 - dehydrobudesonide	N.D.	N.D.	N.D.	N.D.
S - 11 - keto budesonide	0.023	0.025	0.027	0.031
R - 11 - keto budesonide	0.027	0.028	0.030	0.036
S - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.
R - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.
Total Known	0.00	0.053	0.054	0.051
Mean of Total Knowns	0.027		0.053	
Unknown 1 RRT 1.78	0.055	0.056	0.040	0.056
Unknown 2 RRT 2.13	N.D.	N.D.	N.D.	N.D.
Max Unknown	0.055 RRT 1.78	0.056 RRT 1.78	0.040 RRT 1.78	0.056 RRT 1.78
Total Unknown	0.055	0.056	0.00	0.056
Mean of Total Unknowns	0.056		0.028	
Total Impurities	0.055	0.109	0.054	0.107
Mean of Total Impurities	0.082		0.081	

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Continued from page number

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Temp Study

150 µg

75 mg/ml ¹ Concentrate	Control		Heated at 121°C for 20Mins	
	D1	D2	D3	D4
16α Hydropredisalone	0.047	0.048	0.059	0.055
Desonide	N.D.	N.D.	N.D.	N.D.
21 - Dehydro - budesonide	0.025	0.031	0.028	0.034
Budesonide - 12 - dihydro	0.022	0.024	0.025	0.029
22 - Methyl - Homologue of Budesonide	0.031	0.031	0.047	0.040
D - homobudesonide	0.021	0.021	0.020	0.020
14, 15 - dehydrobudesonide	N.D.	N.D.	N.D.	N.D.
S - 11 - keto budesonide	0.021	0.023	0.023	0.023
R - 11 - keto budesonide	0.026	0.030	0.030	0.032
S - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.
R - 21 - acetate budesonide	N.D.	N.D.	N.D.	N.D.
Total Known	0.00	0.00	0.059	0.055
Mean of Total Knowns	0.00		0.057	
Unknown 1 RRT 1.78	0.052	0.051	0.042	0.045
Unknown 2 RRT 2.13	N.D.	N.D.	N.D.	N.D.
Max Unknown	0.052	0.051	0.042	0.045
Total Unknown	RRT 1.78 0.052	RRT 1.78 0.051	RRT 1.78 0.042	RRT 1.78 0.045
Mean of Total Unknowns	0.052		0.044	
Total Impurities	0.052	0.051	0.059	0.055
Mean of Total Impurities	0.052		0.057	

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Temp Study

	Brand
16α	0.041
Hydroprednisolone	
Desonide	N.D.
21 - Dehydro - budesonide	0.209
Budesonide - 12 - dihydro	0.071
22 - Methyl - Homologue of Budesonide	0.065
D - homobudesonide	N.D.
14, 15 - dehydrobudesonide	N.D.
S - 11 - keto budesonide	N.D.
R - 11 - keto budesonide	0.132
S - 21 - acetate budesonide	N.D.
R - 21 - acetate budesonide	N.D.
Total Known	0.477
Unknown 1 RRT 1.78	N.D.
Unknown 2 - RRT 2.13	N.D.
Max Unknown	N.D.
Total Unknown	0.00
Total Impurities	0.477

PLS

Conclusion

Temperature stress produces results which indicate
no degradation due to stress.

Degradant ^{PL 1.9 Sept} levels are below those
observed in brand product,

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N/A PL.